This report is required by law (7 USC 2143). Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 21

See attached form for additional information.

Interagency Report Control No.:

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY

(TYPE OR PRINT)

1. CERTIFICATE NUMBER: 93-R-0026
CUSTOMER NUMBER: 1182

FORM APPROVED
OMB NO. 0579-0036

S R I International
333 Ravenswood Avenue
Menlo Park, CA 94025

Telephone: (b)(6), (b)(7)c

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, or experimentation, or held for these purposes. Attach additional sheets if necessary)

FACILITY LOCATIONS (Sites) - See Atached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (Attach additional sheets if necessary or use APHIS Form 7023A)

A. Animals Covered By The Animal Welfare Regulations	B. Number of animal being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not ye used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use o pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals an for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for wh the use of appropriate anesthetic, analgesic, or tranquiliz drugs would have adversely affected the procedures, res or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasc such drugs were not used must be attached to this repor	F. TOTAL NUMBER OF ANIMALS (COLUMNS C + D + E)
4. Dogs		310	70	4	384
5. Cats					
6. Guinea Pigs					
7. Hamsters		53	60		113
8. Rabbits	6	187		1	188
9. Non-human Primates					
10. Sheep					
11. Pigs					
12. Other Farm Animals					
13. Other Animals					

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anestetic, analgesic, and tranquilizing drugs, prior to, during, and following actual rese teaching, testing, surgery, or experimentation were followed by this research facility.

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and app Institutional Animal Care and Use Committee (IACUC). **A summary of all such exceptions is attached to this annual report.** In addition to identifying the IACUC-approved exceptions, this summary in brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL
(Chief Executive Officer or Legally Responsible Institutional Official)

(b)(6), (b)(7)c

NAME & TITLE OF C.E.O. OR INSTITUTIONAL OFFICIAL (Type or Print)
(b)(6), (b)(7)c

DATE SIGNED
11/21/05

APHIS FORM 7023 (Replaces VS FORM 18-23 (OCT 88), which is obsolete.)
(AUG 91)

NOV 25 2005

Column E Explanation

1. Registration Number: 93-R-0026
2. Number of animals used in these studies: 5
3. Species (common name) of animals used in the study: Dog (4), Rabbit (1)
4. Explain the procedure producing pain and/or distress.

Three of the dogs assigned into Block E were used for a toxicology, [redacted] study. One dog assigned into Block E was used for a [redacted] study. The procedures involved did not cause the category E classification; rather it was the systemic toxicity from the administration of the test articles that caused discomfort to the dogs in this category. The three Block E dogs assigned to the dose range-finding study were dosed daily for four days and exhibited intermittent reactions including slight emesis, and loose stool. Dosing was discontinued on Day 5 when adverse reactions were observed, including dyspnea, and marked hypoactivity. One female was humanely euthanized on Day 5. One male was euthanized on Day 6. The third dog was euthanized on Day 11 due to lack of appetite (although there was intervention), [redacted]

The 1 dog assigned into Block E, used for a [redacted] study, was dosed iv in order to determine the [redacted] of the test article when compared with oral administration. The drug was administered over a slightly extended, 3 minute bolus. The dog began to exhibit adverse reactions post dose and died within 10 minutes of the injection, as euthanasia was being prepared. No analgesic or other drugs were given to the dogs since the use of drugs may have interfered with the [redacted] of the compound being tested, and ultimately interfere with the interpretation of the study results and the toxicity assessment of the test article.

The 1 rabbit assigned to block E was used in a [redacted] study. The objective of the study was to determine the [redacted] and relevant parameters after administration of a single oral dose, split oral dose, or single iv injection. Oral dose is the intended route proposed for clinical use. Intravenous injection was necessary to determine the [redacted] of the compound. The rabbit was administered a single bolus (over 3 minutes) injection. Adverse signs were not observed until after the rabbit was returned to its cage where it [redacted] and died as observations were being made.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results. (For Federally mandated testing, see Item 6 below)

The purpose of the toxicology [redacted] study was to determine the [redacted] of the test compound and to evaluate toxicity after administration of a single iv dose in dogs. The minimum number of animals was used to conduct the range finding study. The dogs that developed adverse clinical signs were euthanatized. Animal

All redactions on this page are pursuant to (b)(4).

welfare concerns were taken into consideration to ensure that the dogs did not experience pain, discomfort or distress beyond what was necessary to obtain scientifically valid results.

The purpose of the [redacted] study was to determine if the therapeutic drug, delivered intravenously, could provide bioavailability data of suitable quality and integrity for FDA applications. The iv administration was not predicted to cause adverse reactions and was not anticipated. As previously mentioned, animal welfare was ensured. Taking into consideration the necessity for collection of scientifically valid data, the distress exhibited by the rabbit assigned to Block E in this study, was not expected.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g., APHIS, 9 CFR 113.102):

Agency: Food and Drug Administration (FDA) [redacted]

An Investigational New Drug (IND) submission requires: A summary of the pharmacological and toxicological effects of the drug in animals.